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THE EFFECT OF SMOKING TOBACCO ON THE CARDIOVASCULAR SYSTEM

PART II

PERIPHERAL BLOOD VESSELS

The existence of vasoconstriction of the peripheral blood vessels may be determined by a decrease of the cutaneous temperatures of the extremities or by a decrease of the velocity of blood flow of the peripheral vessels of the extremities as measured by the plethysmograph. Definite vasoconstriction of the peripheral blood vessels as evidenced by a decrease of the cutaneous temperatures of the extremities has been reported to result from the smoking of tobacco by Maddock and Coller,[24] Barker,[25] Wright and Moffat,[26] Johnson and Short,[27] Lampson,[28] and Moyer and Maddock.[29] With the exception of Shulman and Mulinos[30] investigators generally have reported that smoking of tobacco causes a decrease of peripheral blood flow, as measured by the plethysmograph. Shulman and Mullinos[30] attributed the decrease in blood flow to deep breathing. Similarly Smithwick[31] reported that blood flow through the fingers was decreased by immersion of the contralateral hand in cold water, by a loud noise or even by an unpleasant thought. On the other hand, Weatherby[32] found that altered respiratory movements associated with smoking were of relatively little importance in bringing about the fall of cutaneous temperature of the extremities. However, it was necessary to avoid other physiologic and psychic stimuli.

To determine whether the mechanical act of smoking was a factor in the production of vasoconstriction of the peripheral blood vessels, study of persons puffing on an unlighted cigaret, paper tube or empty pipe and smoking nicotine-free cigarets was carried out by Maddock and Coller,[24] Wright and Moffat,[26] Moyer and Maddock,[29] Weatherby,[32] Evans and Stewart,[33] and Roth, McDonald and Sheard.[34] Negligible changes in the skin temperature, blood pressure and pulse rate occurred. At this point a word might be said about English filter holders. Moyer and Maddock[29] and Roth, McDonald and Sheard[34] have shown that the filtering process of these holders is not adequate to prevent lowering of the cutaneous temperatures of the extremities and Segal[35] pointed out that lowering of the T waves electrocardiographically was not prevented.

Barker[25] in 1933 presented evidence that the effect of smoking on the peripheral blood vessels was due to the absorbed portion of the tobacco smoke and not to the cigaret paper. Roth, McDonald and Sheard[34] confirmed this observation in 1944.

TOXIC SUBSTANCES IN TOBACCO SMOKE AND EFFECTS PRODUCED UNDER VARYING CONDITIONS

Other investigators have shown that the substances contained in tobacco smoke absorbed by the body are pyridine bases, carbon monoxide and nicotine. The pyridine compounds are irritating to the mucous surface but for the most part the amounts absorbed are too small to be of any physiologic interest.

Baumberger[36] studied the effect of carbon monoxide in the tobacco smoke and felt that it was extremely unlikely that the carbon monoxide of tobacco smoke was injurious to any but the most inveterate smokers. Other investigators have found that the average saturation of carbon monoxide in the blood of smokers who inhaled was about 5 per cent in contrast to the 20 per cent saturation necessary to cause disagreeable symptoms among normal persons. However, Barach, Eckman and Molomut[37] called attention to the fact that pilots in whom the hemoglobin of the blood has a carbon monoxide saturation of from 5 to 10 per cent as a result of smoking may aggravate the oxygen want in the tissues when flying at an altitude of 10,000 to 12,000 feet without oxygen.

Ever since nicotine was isolated in 1828, it has been regarded as the most toxic substance in tobacco smoke. Traube[38] first studied the effect of nicotine on the dog's heart and found that there was first a slowing or even a temporary arrest followed by tachycardia with reinforced contractions. In 1938 Thienes and Butt[39] demonstrated greater vascular degeneration in their control animals than in their animals chronically poisoned with nicotine. Because of insufficient control studies they felt that much of the previous experimental and clinical data concerned with vascular degeneration due to chronic nicotine poisoning was of doubtful value.

To determine whether nicotine or tobacco produced vasoconstriction of the coronary arteries, Laubry, Walser and Deglaude[40] measured the coronary flow in isolated rabbit hearts and found that nicotine in small amounts actually increases the coronary flow and that toxic doses were necessary to produce vasoconstriction. Likewise, Mansfeld and Hecht[41] introduced tobacco smoke into the lungs of the heart-lung preparation of dogs and found only coronary dilatation and increased cardiac output.

Haag[42] demonstrated in animals that rises of blood pressure which were produced by intravenous injections of smoke solutions were proportional to the nicotine content of the solution.

Moyer and Maddock[29] and others have pointed out that the form in which the tobacco is smoked also determines the amount of nicotine available for absorption; the largest amount per unit of weight is obtained from cigars and pipes and the smallest from cigarets. This result is due to the more nearly complete combustion of the nicotine in the cigaret. Also, the drier the tobacco smoked, the better the combustion and the smaller the nicotine content of the smoke. Baumberger[43] has estimated that approximately 2.52 mg. of nicotine is assimilated by a noninhaler and 3.33 mg. by an inhaler when one cigaret is smoked. Recently Haag and Larson[44] have carried out studies on a new "low nicotine" tobacco which when it is smoked produced much less pronounced effects on blood pressure and pulse rate than that produced by ordinary cigaret tobacco.

Maddock and Coller[24] and Moyer and Maddock[29]

presented evidence that the vasoconstriction produced by smoking cigarets of standard brands was analogous to that produced by the intravenous injection of as much nicotine as was contained in the cigaret smoked. Furthermore, they as well as Wright[36] and others noted that smoking cigarets which did not contain nicotine produced no appreciable effects on the cutaneous temperature of the extremities. Johnston[45] in England added support to the nicotine theory in that he assumed that smoking of tobacco is essentially a means of administering nicotine. He felt that smokers showed the same attitude toward tobacco as addicts did to a particular drug. He gave nicotine both hypodermically and intravenously and derived the same response as from the inhalation of tobacco smoke.

Weatherby[32] in 1942 found that vasoconstriction took place after smoking standard brands of cigarets but when denicotinized cigarets were smoked the vasoconstriction was abolished almost completely. Restoration of the original nicotine content to such cigarets restored the original effects. This observation indicates that nicotine is the most important agent which contributed to the circulatory and cutaneous changes.

In contrast, Evans and Stewart found a similar decrease in peripheral blood flow with reduction of the cutaneous temperatures of the extremities as a result of smoking standard brands of cigarets, denicotinized cigarets or cigarets containing no nicotine (cornsilk). They attributed these changes to the sympathetic stimulation which was brought about by the irritating effect of smoke on the respiratory tract and not to the nicotine content of the cigarets.

Goetz[42] concluded from his studies that smoking causes a diminution in the peripheral blood flow which is brought about in a two fold manner: first by reflex stimulation arising from the irritating effect of smoke on the respiratory tract and lung and later by the pharmacologic action of nicotine absorbed and accumulated during smoking.

McDonald, Sheard and I confirmed the earlier observations of Maddock and Coller[24] and Moyer and Maddock[29] in regard to the peripheral vasoconstriction produced by both smoking of cigarets and by intravenous injection of a similar amount of nicotine. In addition we compared for the first time the effect of smoking a standard brand of cigarets and the intravenous injection of a similar amount of nicotine on the electrocardiographic tracings of normal subjects and found them strikingly similar. Even habitual smokers demonstrated physiologic changes to smoking of tobacco.

SUMMARY

From the foregoing evidence a tentative summary of the effect of smoking of tobacco on the cardiovascular system may be made as follows: in some persons smoking of tobacco produces pain somewhat similar to angina pectoris; there is some suggestion that in many such persons smoking produces a rise in blood pressure preceding the onset of the pain; the pain produced by smoking can be distinguished from angina pectoris by its greater violence and a longer duration, by a lack of relation to exercise, its occurrence at rest and by the absence of facial blanching or changes in pulse rate during the attack.

Numerous investigators have demonstrated electrocardiographic changes following smoking of tobacco. These include tachycardia, arrhythmia, increased heart rate, lowering or inversion of the T waves and in one case sino-auricular block. In addition, an associated rise in blood pressure is present. Recent evidence points to increased work of the heart as a possible cause of these changes but the effects of stimulation of the sympathetic nerves or paralysis of the parasympathetic nerves cannot be excluded. In some of the cases in which electrocardiographic changes were found, long cessation of smoking resulted in reversion of the electrocardiogram to a normal pattern. While coronary vasoconstriction has been suggested as a possible cause of angina pectoris, some evidence is available to show that small amounts of tobacco or nicotine actually increased the coronary flow and that toxic doses are necessary to produce vasoconstriction in the isolated hearts of rabbits.

The evidence of most investigators points to vasoconstriction of the peripheral blood vessels as a result of smoking of tobacco. Even habitual smokers who presumably have a tolerance to tobacco showed this effect. Apparently the vasoconstriction of the peripheral blood vessels produced by smoking cigarets is analogous to that produced by a similar amount of nicotine injected intravenously.

Finally, the smoking of tobacco is most likely only a contributory factor in the production of cardiovascular disorders and not an etiologic one. Although considerable evidence at present points to nicotine as the most likely factor in the production of certain functional changes in the cardiovascuar system, further proof will be necessary before this possibility can be accepted.

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REFERENCES

1. Johnson, W. M.: J.A.M.A. 93:665-667 (Aug. 31) 1929. 2. White, P. D. and Sharber, Trimble: J.A.M.A. 102:655-657 (Mar. 3) 1934. 3. Glendy, R. E., Levine, S. A. and White, P. D. J.A.M.A. 109:1775-1781 (Nov. 27) 1937. 4. English, J. P., Willius, F. A. and Berkson, Joseph: J.A.M.A. 115:1327-1328 (Oct. 19) 1940. 5. Willius, F. A.: Proc. Inter-State Postgrad. M. A. North America, 1942, pp. 308-310. 6. Neuhof, Selian: Arch. Int. Med. 17:659-662 (May) 1916. 7. Barrow, W. H. and Ouer, R. A.: Arch. Int. Med. 71:547-554 (Apr.) 1943. 8. Graybiel, Ashton, Starr, R. S. and White, P. D.: Am. Heart J. 15:89-99 (Jan.) 1938. 9. Allbutt, Clifford: Diseases of the arteries including angina pectoris. London, Macmillan & Co., Ltd., 1915, vol. 2, pp. 244-248. 10. Moschcowitz, Eli: J.A.M.A. 90:733-737 (Mar. 10) 1928. 11. Aikman, John: New York State J. Med. 52:891-897 (Oct. 30) 1915. 12. Golston, H.: Virginia M. Monthly. 64:319-325 (Sept.) 1937. 13. Cornwall, E. E.: M. Times, New York. 62:209-211 (July) 1934. 14. Birk, B. J. and Huber, H. H.: Wisconsin M. J. 38:733-735 (Sept.) 1939. 15. White, P. D.: Heart disease. Ed. 3, New York, The Macmillan Company, 1944, pp. 533-534. 16. Ralli, Elaine P. and Oppenheimer, B. S.: Proc. Soc. Exper. Biol. & Med. 26:9-11 (Oct.) 1928. 17. Langley, G. N., McSwiney, B. A., Mucklow, S. L., Stopford, J. B. and Wilson, S. R.: J. Physiol. 57:vi (Nov. 18) 1922. 18. Harkavy, Joseph: J. Invest. Dermat. 2:257-279 (Oct.) 1939. 19. Sulzberger, M. B.: J.A.M.A. 102:11-16 (Jan. 6) 1934. 20. Green, M. A.: J. Invest. Dermat. 5:179-186 (Aug.) 1942. 21. Maddock, W. G., Malcolm, R. L. and Coller, F. A.: Am. Heart J. 12:46-52 (July) 1936. 22. Trasoff, A., Blumstein, George and Marks, Myer: J. Allergy. 7:250-253 (Mar.) 1936. 23. Westcott, F. H. and Wright, I. S.: J. Allergy. 9:555-564 (Sept.) 1938. 24. Maddock, W. G. and Coller, F. A.: Ann. Surg. 98:70-81 (July) 1933. 25. Barker, N. W.: Proc. Staff Meet., Mayo Clin. 8:284-287 (May 10) 1933. 26. Wright, I. S. and Moffat, Dean: J.A.M.A. 103:318-323 (Aug. 4) 1934. 27. Johnson, H. J. and Short, J. J.: J. Lab. & Clin. Med. 19:962-966 (June) 1934. 28. Lampson, R. S.: J.A.M.A. 104:1963-1966 (June 1) 1935. 29. Moyer, C. A. and Maddock, H. G.: Arch. Surg. 40:277-285 (Feb.) 1940. 30. Shulman, Israel and Mulinos, M. G.: Am. J. Physiol. 126:629-630 (July 1) 1939. 31. Smithwick, R. H.: Arch. Surg. 40:286-306 (Feb.) 1940. 32. Weatherby, J. H.: Am. Heart J. 24:17-30 (July) 1942. 33. Evans, W. F. and Stewart, H. J.: Am. Heart J. 26:78-91 (July) 1943. 34. Roth, G. M., McDonald, J. B. and Sheard, Charles: J.A.M.A. 125:761-767 (July 15) 1944. 35. Segal, H. L.: Am. J. M. Sc. 196:851-861 (Dec.) 1938. 36. Baumberger, J. P.: J. Pharmacol. & Exper. Therap. 21:23-34 (Feb.) 1923. 37. Barach, A. L., Eckman, Morris and Molomut, Norman: Am. J. M. Sc. 202:336-341 (Sept.) 1941. 38. Traube, L.: Allg. med. Centr.—Ztg. 31:821-825, 1862. 39. Thienes, C. H. and Butt, E. M.: Am. J. M. Sc. 195:522-529 (Apr.) 1938. 40. Laubry, Ch., Walser, J. and Degiaude, L.: Bull. Acad. de méd., Paris. 109:595-598 (Apr. 25) 1933. 41. Mansfeld, G. and Hecht, Katharina: Arch. f. exper. Path. u. Pharmakol. 172:362-372, 1933. 42. Haag, H. B.: J. Lab. & Clin. Med. 25:610-618 (Mar.) 1940. 43. Baumberger, J. P.: J. Pharmacol. & Exper. Therap. 21:35-46 (Feb.) 1923. 44. Haag, H. B. and Larson, P. S.: Science. n. s. 97:187-188 (Feb. 19) 1943. 45. Johnston, L. M.: Lancet. 2:742 (Dec. 19) 1942. 46. Goetz, R. H.: Clin. Proc. Cape Town, South Africa. 1:190-203 (June) 1942.

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